Categorizing chlordecone potential degradation products to explore their environmental fate

Pierre Benoit, Laure Mamy, Rémi Servien, Ziang Li, Eric Latrille, Virginie Rossard, Fabienne Bessac, Dominique Patureau, Fabrice Martin-Laurent

Categorizing chlordecone potential degradation products to explore their environmental fate

Pierre Benoit[a,*], Laure Mamy[a], Rémi Servien[b], Ziang Li[a], Eric Latrille[c], Virginie Rossard[c], Fabienne Bessac[d], Dominique Patureau[c], Fabrice Martin-Laurent[e]

[a] *UMR ECOSYS, INRA, AgroParisTech, Univ. Paris-Saclay, 78850 Thiverval-Grignon, France*

[b] *UMR TOXALIM, INRA, Univ. de Toulouse, 31027 Toulouse, France*

[c] *LBE, INRA, 11100 Narbonne, France*

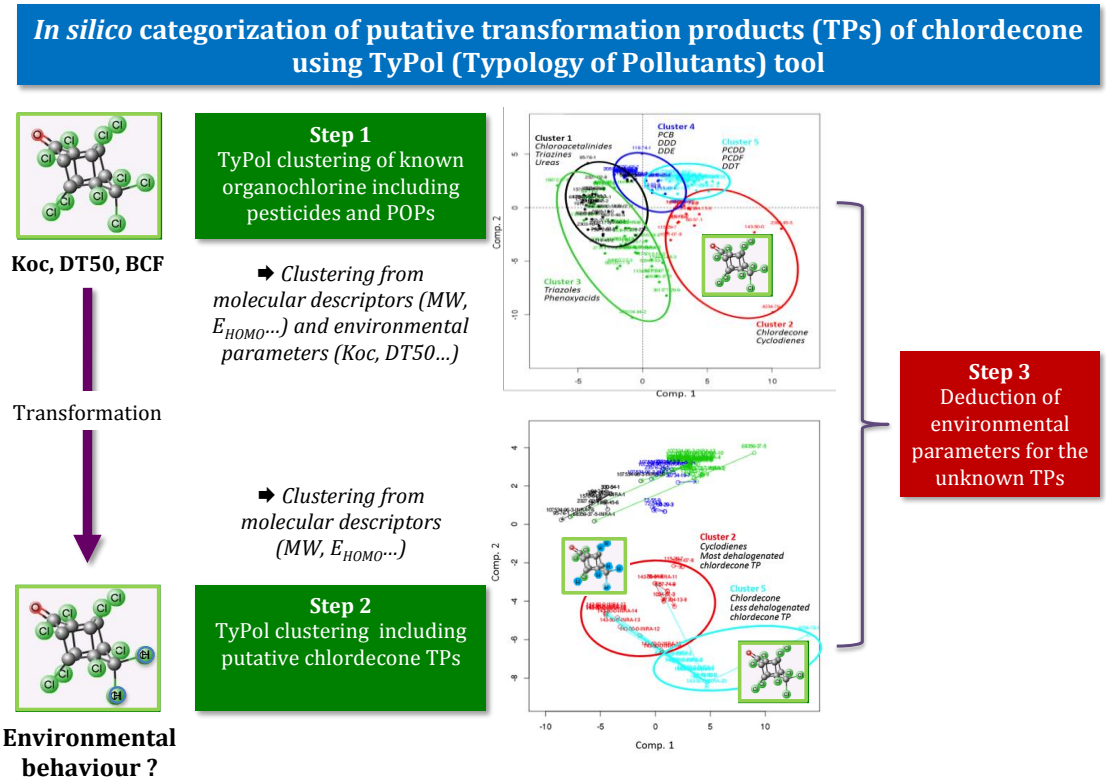
[d] *INPT-Ecole d'Ingénieurs de Purpan, Univ. de Toulouse, 31076 Toulouse, France ; CNRS/Univ. De Toulouse (Paul Sabatier)-UMR 5626, Laboratoire de Chimie et Physique Quantiques, 31062 Toulouse, France*

[e] *UMR AgroEcologie, INRA, AgroSup Dijon, Univ. Bourgogne Franche-Comté 21065 Dijon, France*

Corresponding author.

E-mail address: pierre.benoit@grignon.inra.fr (P. Benoit)

GRAPHICAL ABSTRACT



ABSTRACT

Chlordecone ($C_{10}Cl_{10}O$; CAS number 143-50-0) has been used extensively as an organochlorine insecticide but is nowadays banned and listed on annex A in The Stockholm Convention on Persistent Organic Pollutants (POPs). Although experimental evidences of biodegradation of this compound are scarce, several dechlorination products have been proposed by Dolfing et al. (2012), using Gibbs free energy calculations to explore different potential transformation routes. We here present the results of an *in silico* classification (TyPol - Typology of Pollutants) of chlordecone transformation products (TPs) based on statistical analyses combining several environmental endpoints and structural molecular descriptors. Starting from the list of putative chlordecone TPs and considering available data on degradation routes of other organochlorine compounds, we used different clustering strategies to explore the potential environmental behaviour of putative chlordecone TPs from the knowledge on their molecular descriptors. The method offers the possibility to focus on TPs present in different classes and to infer their environmental fate. Thus, we have deduced some hypothetical trends for the environmental behaviour of TPs of chlordecone assuming that TPs, which were clustered away from chlordecone, would have different environmental fate and ecotoxicological impact compared to chlordecone. Our findings suggest that mono and di-hydrochlordecone, which are TPs of chlordecone often found in contaminated soils, may have similar environmental behaviour in terms of persistence.

Keywords: Organochlorine pesticides, Biodegradation, Molecular modeling, Partial least squares

HIGHLIGHTS

- TyPol, an *in silico* typology, was used to categorize 170 organochlorine molecules
- Clustering used both molecular descriptors and environmental behaviour
- Parent and transformation products represented various chemical families
- 20 chlordecone putative transformation products (TPs) were categorized
- Combining two clustering allowed assessing the potential fate of chlordecone TPs

1. Introduction

In the French West Indies (FWI), chlordecone ($C_{10}Cl_{10}O$; CAS number 143-50-0 - decachlorooctahydro-1,3,2-metheno-2Hcyclobuta[c,d]pentalen-2-one) has been largely used on banana plantations over the 1978–1993 period to control banana weewil. Its persistence in the agricultural soils of the FWI (i.e., 20,000 ha that represent up to 25 % of the agricultural surface of the FWI) was estimated to last for several decades in Nitisol, centuries in Ferralsol, and half a millennium in Andosol soils (Cabidoche et al., 2009).

This organochlorine insecticide is now banned and listed in annex A of the Stockholm Convention on Persistent Organic Pollutants (POPs) but its former use has induced a general and important contamination of rivers, springs, and drinking water as well as coastal ecosystems of the FWI (Coat et al., 2011) as revealed by investigation of the French National Action Plan for chlordecone (PNAC 2008–2010). In such context, finding strategies to remediate and/or mitigate this contamination on the very long-term is a great challenge and, from this point of view, the FWI represent an open field for remediation (Cabidoche and Jeannoyer, 2011; Levillain et al., 2012).

There is no clear cut evidence of microbial chlordecone degradation under aerobic conditions. Indeed Orndorff and Colwell (1980) proposed that *Pseudomonas aeruginosa strain KO3* and a bacterial consortium isolated from Hopewell plant sewage sludge under aerobic conditions transform chlordecone into monohydro-chlordecone and di-hydro-chlordecone. However, these results have been criticized by Cabidoche et al. (2009) because the initial contents in mono-hydro- and di-hydro-chlordecone, known to be by-products of the synthesis contaminating the chlordecone, have not been measured. This lack is compromising the proposed results because detection of chlordecone TPs can be the result of incomplete chlorination of chlordecone during synthesis and not to microbial biodegradation. Later on, George and Claxton (1988) studied chlordecone degradation catalyzed by three *Pseudomonas* spp. showing that after two weeks of incubation chlordecone reached only 15–25% of initial concentration with a relatively high uncertainty of 10% on chlordecone HPLC concentration measurements. In addition, in non-inoculated control, mono- and dihydro chlordecone were detected as well. A poor bacterial growth was recorded and, consequently, the authors concluded that due to its important chlorination, chlordecone was a poor carbon source for bacterial growth. However, a recent study based on a large data set of 881 field soils of the FWI showed a significant increase of the

5bhydrochlodecone/chlordecone ratio in the soils 25 times greater than in commercial formulations which suggested that natural transformation into 5b-hydrochlodecone over the long term occurred in these soils (Devault et al., 2016).

Under anaerobic conditions, a pure culture of *Methanosarcina thermophila* grown on acetate was shown to convert chlordecone to polar and nonpolar products (Jablonski et al., 1996). Interestingly, similar pattern of soluble chlordecone decomposition products were obtained with reduced vitamin B12 and reduced coenzyme F430 isolated from *M. thermophila*. More recently, *Pseudonocardia* sp. KSF27 isolated from a soil repeatedly treated with endosulfan was shown to also degrade dieldrin and other organochlorine insecticides such as chlordecone but without providing information on the degradation pathway (Sakakibara et al., 2011).

In France, giving the environmental and health problem caused by chlordecone contamination in the West Indies, several research programs have recently been carried out on soil bioremediation. Search for chlordecone-degrading microorganisms under anaerobic and aerobic conditions remains a big challenge due to the lack of experimental evidences of degradation products in soil environment. Indeed, only few measured data on the identification of chlordecone TPs are available showing traces of the TP 5b-hydrochlodecone in some Andosol, Nitisol, and Ferralsol soil samples (Devault et al., 2016; Martin-Laurent et al., 2014). Recently, Fernandez-Bayo et al. (2013) gave evidence for a weak but measurable mineralization of ^{14}C-chlordecone in an Andosol from Guadeloupe in aerobic conditions reaching 4.9% of the ^{14}C-chlordecone initially added in the topsoil (0-20 cm) and 3.2% in the below horizon (30-60 cm) over a 230d period of incubation. The absence of $^{14}CO_2$ evolution in sterile soil microcosms led the authors to conclude that chlordecone mineralization was biotic being most likely catalyzed by microorganisms (Fernandez-Bayo et al., 2013).

Dolfing et al. (2012) conducted a theoretical study using Gibbs free energy calculations to explore the thermodynamic feasibility of different chlordecone potential degradation routes. By performing ab initio quantum chemical calculations to estimate molar values of ΔfHm° and ΔfGm° for chlordecone and selected dechlorination products, they have estimated the energetics of the degradation and dechlorination of chlordecone under a variety of redox conditions. They ended up with the proposal of a list of 20 potential TPs and concluded that there were no thermodynamic reasons why chlordecone-respiring or -fermenting organisms should not exist.

Complementary information could be brought by clustering approaches based on the relationships between molecular properties and environmental fate of organic compounds. With this aim, we recently developed 'TyPol' (Typology of Pollutants), a classification method based on statistical analyses combining several environmental endpoints (i.e. environmental parameters such as sorption coefficient, degradation half-life or bioconcentration factor), and structural molecular descriptors (number of atoms in the molecule, molecular surface, dipole moment, energy of orbitals…). This approach also allows to focus on TPs present in different classes and to infer possible changes in environmental fate consecutively to different degradation processes (Servien et al., 2014). Starting from the list of chlordecone TPs proposed by Dolfing et al. (2012) and considering available literature data on degradation routes of other organochlorine compounds, we conducted a study using TyPol to explore the potential environmental behaviour of chlordecone TPs based on their molecular properties.

2. Materials and methods

2.1. Clustering methodology

The TyPol tool permits to classify organic compounds, and their transformation products, according to both their behaviour in the environment and their molecular properties. The calculation of molecular descriptors is performed using an *in silico* approach, while the environmental endpoints (i.e. environmental parameters) are extracted from several available databases and literature. The strategy relies on partial least squares analysis and hierarchical clustering (see below 2.5. Statistical treatments). The robustness of the TyPol method was assessed on a list of 215 organic compounds using a cross-validation algorithm. The information system is based on a management system for relational database MySQL DBMS-R (version 5.1), an Apache web server (version 2.2), and the statistical R software (also used for graphs). More details concerning TyPol can be found in Servien et al. (2014).

2.2. Environmental parameters

Seven environmental parameters are considered in TyPol in order to cover the main processes involved in the behaviour of organic substances: water solubility (*Sw*) and octanol-water partition coefficient (*Kow*) to describe dissolution; vapor pressure (P_{vap}) and Henry's law constant (K_H) for volatilization from soil and plant, and water, respectively; adsorption coefficient normalized to soil carbon organic content (*Koc*) for

adsorption; half-life (*DT50*) for degradation; and bioconcentration factor (*BCF*) for ecotoxicity (Servien et al., 2014).

2.3. Molecular descriptors

Forty relevant molecular descriptors are considered in TyPol. They have been selected from a literature review of QSARs (Quantitative Structure Activity Relationships) developed to predict different environmental processes (Mamy et al., 2015). We focused on QSARs only built with structural molecular descriptors (number of atoms, molecular surface, dipole moment, energy of the orbitals…) rather than characteristics such as *Sw* or *Kow*. Molecular descriptors are calculated using several software (ChemOffice Ultra 12.0, Dragon 5.5).

2.4. Database implementation

A literature survey was done to provide a list of compounds (parent and transformation product) representing different mechanisms - i.e reductive dechlorination, hydroxylation, oxidation, epoxidation, photolysis, hydrolysis - involved in their abiotic or biotic transformations. In total, 170 chlorinated compounds were listed and added to the TyPol database by implementing data on environmental parameters when available (130 compounds). The idea was to cover a broad spectrum of compounds such as organochlorine pesticides but also PCB, PCDD and PCDF so that clustering could segregate chlorinated compounds according to their molecular properties and environmental behaviour. TPs were looked for these different chemical families (Hester and Harrison, 1996; Roberts and Hudson, 1999). Molecular descriptors were calculated and inserted for each compound. For chlordecone, 20 dechlorinated TPs proposed by Dolfing et al. (2012) as well as chlordecol were considered.

2.5. Statistical treatments

In TyPol, the PLS (Partial Least Squares) model is carried out to find the multidimensional directions in the X observable variables (i.e. molecular descriptors) space that explains the maximum multidimensional variance direction in the Y predicted variables (i.e. environmental parameters) space. The optimal number of PLS components to perform clustering is selected according to Wold rules (Wold, 1978). In addition, we use the NIPALS (Non-linear Iterative PArtial Least Squares) algorithm, which allows performing PLS without removing the individuals with missing values

and without estimating these missing values (Tenenhaus, 1998). After PLS analysis, a hierarchical clustering algorithm is used on the X and Y PLS axes to categorize the molecules by assignment of similar compounds into one cluster. At each step, the final number of clusters is chosen by comparison of heights in the dendrogram, a statistical map resuming Ward clustering. Minimization of intra-variability and maximization of inter-variability are the parameters retained to choose the most appropriate number of clusters (Servien et al., 2014).

We used TyPol in two manners. In a first approach, TyPol was used to identify relationships between molecular descriptors and environmental fate processes among several clusters of organochlorine molecules by considering molecular descriptors and available environmental parameters. In a second approach, TyPol clustering was performed by including chlordecone TPs and using only the molecular descriptors as their environmental parameters are unknown. In this case the observable and the predicted variables are the same (i.e the molecular descriptors) and the PLS is equivalent to a Principal Component Analysis (PCA). The clustering was further used to estimate trends for the environmental parameters of chlordecone TPs clusters by comparing molecular descriptors of chlordecone TPs to those of 113 other organochlorine compounds of the database and 16 organochlorine TPs for which environmental parameters such as sorption coefficient or degradation half-life were known. The dataset generated allowed discussing and proposing hypothetical environmental behaviour of the different chlordecone TPs.

3. Results and discussion

3.1. Degradation routes of organochlorine pesticides

As reviewed by Roberts and Huston (1999), organochlorine insecticides such as DDT and cyclodienes were historically among the first major classes of synthetic chemicals that have been restricted because of their high persistence, high potential of bioaccumulation and ubiquitous contamination. Main degradation pathways of these compounds reported in literature are oxidation, epoxidation and dechlorination reactions (Table 1).

The most important transformation reactions in soils of DDT are dehydrochlorination to DDE and reductive dechlorination to DDD. Due to their recalcitrance, these two TPs are still frequently found in environmental samples although they can also undergo

reductive dehalogenation (Subba-Rao and Alexander, 1985) or hydroxylation of aliphatic moieties (Bumpus and Aust, 1987).

Cyclodiene insecticides share few structural similarities with the bishomocubane structure, which constitutes the skeleton of chlordecone and of its derivatives (Francis and Metcalfe, 1984). Chlordane has a variety of metabolic pathways including oxidation, reductive dechlorination, hydroxylation and epoxidation in soils leading to TPs such as dichlorchlordene, oxychlordane, heptachlor, heptachlor epoxide or chordene chlorohydrin (Table 1). Endosulfan is readily hydrolysed in water to the diol form but it is moderately persistent in soil where the major TP is the endosulfan sulfate, which is more persistent than the parent compound.

Up to now, mostly 5b-hydrochlodecone and dihydrochlordecone have been identified as chlordecone TPs mostly concerned (Martin-Laurent et al., 2014; Orndorff and Colwell, 1980) suggesting that in the soil environment hydroxylation and dechlorination are the most probable transformation reactions. The bishomocubane structure (typical for chlordecone and congeners) provides a great stability due to the 10 Cl atoms which promotes electron delocalization and limits the possibilities of oxidation of the C atoms, explaining the great recalcitrance of chlordecone in aerobic conditions. On the contrary, the high chlorine content of the chlordecone molecule makes anaerobic dechlorination the most likely mode of initial transformation reaction (Table 1) as already shown for an important number of different aromatic and aliphatic compounds, including chlorinated ethylenes, PCBs, dioxins and furans, which are degraded by reductive dechlorination (Field and Alvarez, 2008 a and b; Schanke and Wackett, 1992). Dechlorination of chlordecone may occur in reductive environmental conditions and is the most probable route according to thermodynamic approach based on Gibbs free energy calculations (Dolfing et al., 2012).

3.2. Clustering using molecular descriptor and environmental parameters

One hundred and thirty organochlorine compounds were used in this first clustering (Fig.1, Table A1). The number of PLS components was chosen equal to four according to Wold rules (Wold, 1978). The PLS model was characterized by the following statistical results: R^2_X = 0.62, R^2_Y = 0.70 and Q^2_Y = 0.40 indicating that it was a satisfactory model representative for the different compounds included in TyPol. The main characteristic of the first component, which explains 34% of the variance of the molecular descriptors and 47% of the variance for the environmental parameters, is the

strong positive loadings for all the geometric and topological descriptors, and constitutional descriptors like the number of chlorine or halogen atoms (Fig. 2). A contrario, the dipole moment and the total energy have strong negative effects therefore have an opposite effect. The second axis explains 28% of the variance of the molecular descriptors and 23% of the variance for the environmental parameters. On this axis, variables such as the number of chlorine or halogen atoms have a positive loading whereas the number of rotatable, double or simple bonds or the number of hydrogen, oxygen or total atoms have a negative loading (Fig. 2). Fig. 2 also shows that many variables seem to be correlated, mainly the different connectivity and valence connectivity indices.

The selection of the number of clusters was performed by plotting the heights of the dendrogram's node and looking for a break. The results showed that the best choice, minimizing intra-variability and maximizing inter-variability, was to classify the compounds in 5 clusters. The size of the five clusters varied from 15 to 32 compounds (Fig. 1, Table A1), each cluster being characterized by specific features. Fig. 3 shows the range of variations of the values of the 7 environmental parameters for each of the 5 clusters. The trigger value of P_{vap} is indicated to differentiate volatile and non-volatile compounds (there is no trigger value for K_H, FOCUS, 2008), that of *Koc* to differentiate mobile and non-mobile compounds (Mackay, 2006), that of *DT50* to differentiate persistent and non-persistent compounds (1107/2009 EC, 2009), and that of *BCF* to differentiate compounds having or not a potential of bioaccumulation (1107/2009 EC, 2009) (Fig. 3). Depending on the values of P_{vap}, *Koc*, *DT50* and/or *BCF*, each of the five clusters aggregate various organochlorine compounds having (or not) risks for air, water and/or soil contamination and/or high ecotoxicity. The importance of the different environmental parameters in the clustering can be evaluated on the correlation circle (Fig. 2) showing that *BCF*, *Kow* (positive loadings) and *Sw* (negative loading) are strongly related to the first component. P_{vap} and K_H have a positive loading on the second axis. *DT50* and *Koc* are the parameters which have low influence on the two main PLS components of the clustering (Fig. 2)

The cluster 1 contains 31 molecules and groups together chloroacetanilides, chlorinated *s*-triazines, ureas and triallates inputted in TyPol. This cluster is made of compounds characterized by an important dipole moment and high values of total energy, whereas polarizabilities and the different connectivity indices are low (Table A2). These compounds have low number of chlorine atoms, low molecular weight and

low Connolly molecular surface area. Median values of *Sw* are high (median $\log_{10}Sw$ = 1.55) although *Koc* have medium to relatively high values (median $\log_{10}Koc$ = 2.34). They have low *DT50* (Fig. 3) suggesting that they have a low persistence in the environment (Regulation EC 1107/2009, 2009). They also have relatively low *BCF* suggesting that these compounds are not susceptible to bioaccumulate in living organisms (i.e. low ecotoxicity, Regulation EC 1107/2009, 2009). Finally, compounds gathered in cluster 1 have medium K_H values (i.e. a medium volatility from water) but relatively high values of P_{vap} so high volatility from soil and plant, and potential of transfer to atmosphere (FOCUS, 2008). Few compounds of this cluster are closed to those of cluster 2 in the two X-axes of the PLS, but differences between these molecules are more easily noticeable in the Y-axes of the PLS.

The cluster 2 contains mirex, kelevan and chlordecone as well as other organochlorine pesticides such as aldrin, chlordane, endosulfan, heptachlor and their known TPs such as oxychlordan, heptachlor epoxide, endosulfan sulfate. The 3 bishomocubanes (chlordecone, mirex and kelevan) are relatively detached from the other molecules in the PLS projection. As discussed above, these three compounds have a very particular chemical structure (bishomocubane family) responsible for their high persistence (high *DT50*) in the environment. They have very high values of connectivity or valence connectivity indices, polarizability, molecular weight, number of chlorine and other halogen atoms; and low values of number of multiple bonds, total energy, HOMO energy, dipole moment and medium value for LUMO energy (Table A2). The number of rotatable and aromatic bonds is extremely low. Considering the environmental parameters, they have low *Sw* but rather low *Koc* (median $\log_{10}Koc$ = 1.76), medium to high *BCF* indicating their that is high ecotoxicity towards living organisms, and high K_H (Dolfing et al., 2012; PPDB, 2013) (Fig. 3).

The cluster 3 is composed of 32 compounds with several chemical families represented: triazoles, phenoxyacids, strobilurins, ketones. These compounds have high dipole moment, high polarizability and low total energy. The number of Cl atoms is low whereas the number of O and N atoms is the highest of all clusters. Valence connectivity indices and connectivity indices for zero and first order are high as well as the Connolly molecular surface area (Table A2). These compounds also have low *DT50* (rapid dissipation and low persistence), medium *Koc* (medium mobility), high *Sw* (and low *Kow*), and low *BCF* suggesting their low ecotoxicity (Fig. 3).

The cluster 4 is composed of 25 compounds, most of them being the PCBs inputted in TyPol and some degradation products of DDT (DDE, DDD). This cluster is characterized by low polarizability, low dipole moment and low connectivity indices. The number of Cl atoms is low as well as the number of O and N atoms. The number of aromatic bonds is high (Table A2). It has the lowest DT50 of the five clusters indicating their relatively low persistence in the environment. Compounds of cluster 4 have high values of *BCF* indicating their high ecotoxicity. They also have high *Kow* and low *Sw*, high P_{vap} and K_H, indicating their high potential for volatilization.

The cluster 5 contains 27 molecules with all PCDD and PCDF and few organochlorine insecticides such as DDT. They have high values of polarizability and valence and connectivity indices, whereas the total energy, LUMO energy and the dipole moment are very low. This group is characterized by low number of N and O atoms and by contrast high number of Cl atoms (Table A2). This feature, in combination with high molecular weights and low number of hydrogen atoms is related to low values of *Sw* (the lowest among the 5 clusters) and high values of *Kow*, and to the highest values of *BCF*. The compounds of cluster 5 also have the highest DT50 among the 5 clusters, which means very high persistence in soils (Regulation EC 1107/2009, 2009) (Fig. 4). Finally, they have low values of P_{vap} and K_H indicating a moderate risk of transfer to the atmosphere (Fig. 3).

3.3. Clustering using molecular descriptors only

We have added to the 130 organochlorine compounds inputted in TyPol, the 19 TPs of chlordecone proposed by Dolfing et al. (2012) as well as 21 putative TPs of tebuconazole containing Cl atoms recently screened by Storck et al. (2016) (Table 2). With this new dataset a second TyPol clustering was carried out and four PLS components were selected as described above. The PLS model had good statistical results: R^2 = 0.65, and Q^2 = 0.81. It has to be noted that the PLS analysis was only performed on the molecular descriptors. Therefore, the X observable variables are also the Y predicted variables. Nevertheless, obtained results showed that the PLS was a good model for the different compounds included in TyPol. The first and second components explained 39% and 26% of the variance, respectively. The second PLS is sharing some similarities with the first one. The main characteristic of component 1 was also the strong positive loadings for some topological descriptors such as the different connectivity indices as well as the polarizability and strong negative loading of the total

energy. However, by comparison with the first PLS, the dipole moment and number of chlorine and halogens had no influence on this first component. On the contrary, these variables are well distributed along the second component. On this second axis, variables such as the number of chlorine or halogen atoms have this time a negative loading whereas HOMO energy, the number of hydrogen, oxygen, the number of multiple, aromatic and rotatable bonds have a positive loading (Fig. 4). As for the first PLS, the LUMO energy has a poor influence on the 2 first components.

The size of the five clusters varied from 12 to 50 compounds (Fig. 5, Table A3). Compared to the first classification, several compounds moved from one group to another one most likely due to the fact that environmental parameters were not taken into account. For instance, the cluster 1 still contains phenylureas, triallates and s-triazine pesticides but includes also phenoxyacids and few TPs of tebuconazole and small biphenyls. Also, clustering on molecular descriptors separated better chlordecone and analog cyclodienes (mirex, kelevan) and a large part of the putative TPs from the other organochlorine compounds (Fig. 5; Table A3). All these compounds are now found in cluster 5 whereas they were associated to other organochlorine insecticides in the first classification (cluster 2). This more homogeneous composition of cluster 5 around compounds characterized by a bishomocubane skeleton is probably due to the fact that classification was done only with the molecular descriptors. In comparison to the other organochlorine pesticides (still in cluster 2), the chlordecone cluster has several features in common: low number of multiple bound, no rotatable bound, low dipolar moment and high polarizability (Table A4). But the chlordecone cluster was made of compounds characterized by typical values of the following molecular descriptors: they have the lowest total energy and HOMO energy, the highest connectivity indices, the highest number of Cl atoms and the highest molecular weight of all clusters. Such specificities are in accordance with (i) the results of our first clustering which has shown that such trends of molecular descriptors were associated with high values of *DT50* and *BCF* (clusters 2 and 5 of the first clustering) and (ii) the low biodegradation of chlordecone observed in the environment (Cabidoche et al., 2009; Dolfing et al., 2012; Fernandez-Bayo et al., 2013; Martin-Laurent et al., 2014).

An important result was that the main features of molecular descriptors remain quite similar from one classification to another one. As in the first classification, cluster 1 was characterized by low polarizability values, low connectivity and valences indices, low number of Cl atoms and molecular weight (Table A4). Total energy and dipole moment

had high values. Cluster 2 still contained the organochlorine insecticides and additionally, the more dechlorinated TPs of chlordecone. It kept the main features for the molecular descriptors: high values of connectivity or valence connectivity indices, polarizability, molecular weight, number of chlorine and other halogen atoms; and low values of number of multiple and rotatable bonds, low values of total energy and HOMO energy (Table A4). The dipole moment value was a bit higher than in the first classification. Cluster 3 containing triazoles has now incorporated most of the tebuconazole TPs (Table A3). This group is characterized by high dipole moment, high polarizability and low total energy. The number of Cl atoms was low whereas the number of O and N atoms was the highest of all clusters. Valence connectivity indices and connectivity indices for zero and first order were high as well as the Connolly molecular surface area (Table A4). Cluster 4 now gathered all PCDD, PCDF and the majority of PCBs and DDT (Table A3). Molecular descriptors have kept the main features: low polarizability; low dipole moment; low number of Cl, O and N atoms; high number of aromatic bonds. Compared to the first clustering, polarizability as well as the connectivity indices had now medium values in the cluster 4 (Table A4).

3.4. Exploring the environmental fate of putative chlordecone transformation products

The similarities of molecular descriptors distribution values in the two clustering can be used to deduce parameters for compounds for which environmental parameters are unknown. This is done assuming that compounds gathered in the same cluster on the basis of their molecular descriptors have similar environmental parameters (Storck et al., 2016).

Sixty-two parent-TP couples have been used for the TyPol clustering using only molecular descriptors. 74% of TPs were found in the same cluster than their parent molecule suggesting that most of the TPs may have similar behaviour in the environment than parent compounds from which they derived. For organochlorine pesticide such as DDT and chlordane, TPs were always found in the cluster of the parent molecule (Figure 6). This suggests that their transformation changed neither their molecular properties nor their environmental behaviour.

Concerning chlordecone and its potential TPs, we can notice that TPs gathered in different clusters according to the extent of their dechlorination. When more than 4 Cl atoms were replaced by OH then putative TPs gathered to cluster 2 (penta-hydrochlordecone) or cluster 1 (hepta to nona-hydrochlordecone) and not to cluster 5

like parent compound. In the first case, cluster 2 regrouped organochlorine pesticides such as DDT and chlordane but also compounds such as chlorinated dioxin, furans and high molecular weight PCBs whereas cluster 1 was containing low molecular weight PCBs and pesticides such as 2,4D, dicamba, atrazine and chlortoluron. Less dechlorinated compounds as well as chlordecol, remained in cluster 5 suggesting that mono-hydro to tetra-hydrochlordecone could have strong similarities with chlordecone, mirex and kelevan.

Looking more carefully into the analysis of molecular descriptors of the corresponding clusters of chlordecone (cluster 5), organochlorine insecticides (cluster 2) and low molecular weight and more polar pesticides (cluster 1) showed that median values of molecular descriptors were quite discriminant for these 3 groups (see 3.3. Clustering using molecular descriptors only). Clusters 5 and 2 shared common features such as low dipole moment and high polarizability, low number of multiple bound, no rotatable bound, low total energy and HOMO energy, high connectivity indices, high number of Cl atoms and high molecular weight. But, as pointed out before, the chlordecone cluster had more extreme values for the total energy, connectivity indices, dipole moment and Cl atoms number. On the opposite, molecules of cluster 1 had higher dipole moment, higher total energy, lower polarizability, much lower values of connectivity and valence indices, lower number of Cl atoms and lower molecular weight.

Using the results of the first clustering resulting from the analysis of both environmental parameters and molecular descriptors we deduced some trends by linking molecular descriptors features to values of environmental parameters such as *DT50*, *Koc*, P_{vap} and *BCF* for the clusters obtained for chlordecone, organochlorine insecticides and low molecular weight and more polar pesticides. Based on this deductive approach one could hypothesize that the most dechlorinated chlordecone TPs (hepta to nona-hydrochlordecone) may have environmental properties similar to that of low molecular weight and more polar pesticides: low *DT50* (rapid dissipation), medium *Koc* (medium mobility), high *Sw* (and low *Kow*), and low *BCF* so low ecotoxicity. On the contrary, TPs less heavily dechlorinated such as penta-hydrochlordecone may have like its parent compound very high values of *BCF* and high *DT50*, which means a very long persistence in soils and very high risk for bioaccumulation and transfer all along the food chain. Finally the lowly dechlorinated TPs are close to the parent compound and consequently are expected to exhibit similar trends in terms of environmental fate and

ecotoxicological impacts. They would be characterized by a very long persistence in soils and very high risk for the transfer in the food chain but also in the environment *via* mobility from soil to water compartment through slow leaching processes since the chlordecone cluster is characterized by relatively low *Koc*. As pointed out by Dolfing et al. (2012), reductive dechlorination of chlordecone is thermodynamically favorable, but whether this reaction can proceed at environmentally significant rates and/or at rates, which can sustain growth of organisms catalyzing such reactions, remains unproven yet.

4. Conclusion

We used *in silico* molecular typology to explore the potential fate of putative chlordecone TPs. The TyPol approach applied implied two steps. A first clustering step served to search for possible correlations between molecular descriptors of organochlorine compounds and their environmental parameters covering biodegradation, mobility and bioaccumulation processes. From the calculation of molecular descriptors for a series of existing or putative TPs, we performed a second clustering where the filiation between parent and TPs was accounted for. By comparing the two clustering results, we deduced environmental parameters for chlordecone TPs and discussed hypothetical trends for their environmental behaviour.

Recent experimental studies exploring the degrading capacities of different type of soils and of different soil microorganisms have confirmed that biodegradation of chlordecone is very low and slow. Our findings suggest that lowly dechlorinated TPs such as mono and di-hydrochlordecone, often found in chlordecone-contaminated soils, may have similar environmental behaviour than chlordecone in terms of persistence and transfer in the environment, bioaccumulation and transfer all along the food chain. By contrast, more heavily dechlorinated TPs may have very different environmental parameters more favorable than those of chlordecone but unfortunately, to our best knowledge, the conditions leading to their formation remain unknown.

Acknowledgments

The authors acknowledge the Projet Innovant of the “Environnement et Agronomie” Department of INRA and the AIP DEMICHLORD (Etudes exploratoires de la dégradation microbienne de la chlordécone) of INRA for financial supports, and the

494 FIRE (Fédération Ile-de-France de Recherche sur l'Environnement) for Ziang Li's
495 master grant.
496
497 **References**
498 Bristeau S., Amalric L., Mouvet C., 2014. Validation of chlordecone analysis for native
499 and remediated French West Indies soils with high organic matter content. Anal
500 Bioanal Chem, 406,1073–1080
501 Bumpus J.A., Aust S.D., 1987. Biodegradation of DDT 1,1,1-dichloro-2,2-bis-4-
502 (chlorophenyl)ethane by the white rot fungus Phanerochaete crysosporium. Appl
503 Environ Microbiol 53, 2001–2008.
504 Cabidoche Y-M., Lesueur-Jannoyer M., 2011. Long term pollution of soils in French
505 West Indies: how to manage chlordecone contamination? Innov Agron, 16, 117–133.
506 Cabidoche Y-M., Achard R., Cattan P., Clermont-Dauphin C., Massat F., Sansoulet J.,
507 2009. Long-term pollution by chlordecone of tropical volcanic soils in the French
508 West Indies: a simple leaching model accounts for current residue. Environ Pollut
509 157, 1697–1705.
510 Coat S., Monti D., Legendre P., Bouchon C., Massat F., Lepoint G., 2011.
511 Organochlorine pollution in tropical rivers (Guadeloupe): role of ecological factors
512 in food web bioaccumulation. Environ Pollut 159,1692–1701.
513 Devault D.A., Laplanche C., Pascaline H., Bristeau S., Mouvet C., Macarie H., 2016.
514 Natural transformation of chlordecone into 5b-hydrochlordecone in French West
515 Indies soils: statistical evidence for investigating long-term persistence of organic
516 pollutants. Environ Sci, Poll Res, 23, 81-97.
517 Dolfing J., Novak I., Archelas A., Macarie H., 2012. Gibbs free energy of formation of
518 chlordecone and potential degradation products: implications for remediation
519 strategies and environmental fate. Environ Sci Technol 46, 8131–8139.
520 Fernández-Bayo J.D., Saison C., Voltz M., Disko U., Hofmann D., Berns A.E., 2013.
521 Chlordecone fate and mineralisation in a tropical soil (andosol) microcosm under
522 aerobic conditions. Sci Total Environ 463–464, 395–403.
523 Field J.A., Sierra-Alvarez R., 2008a. Microbial degradation of chlorinated dioxins
524 Chemosphere 71, 1005–1018.
525 Field J.A., Sierra-Alvarez R., 2008b. Microbial degradation of polychlorinated
526 biphenyls. Environmental Pollution 155, 1-12

527 Francis B.M., Metcalf R.L., 1984. Evaluation of mirex, photomirex and chlordecone in
528 the terrestrial aquatic laboratory model ecosystem. Environ Health Perspect, 54, 341–
529 346.
530 George, S.E., Claxton, L.D., 1988. Biotransformation of chlordecone by *Pseudomonas*
531 species. Xenobiotica 18, 407–416.
532 Hester R.E., Harrison R.M., 1996. Chlorinated Organic Micropollutants. *Issues in*
533 *Environmental Science and Technology, 6.* The Royal Society of Chemistry,
534 Information Services Cambridge, UK.
535 Jablonski P.E., Pheasant D.J., Ferry J.G., 1996. Conversion of Kepone by
536 *Methanosarcina thermophila*. FEMS Microbiol Lett 139(2–3), 169–173.
537 Levillain J., Cattan P., Colin F., Voltz M., Cabidoche Y-M., 2012. Analysis of
538 environmental and farming factors of soil contamination by a persistent organic
539 pollutant, chlordecone, in a banana production area of French West Indies. Agric
540 Ecosyst Environ 159, 123–132.
541 Mackay, D.S.-C., 2006. Handbook of physical-chemical properties and environmental
542 fate for organic chemicals. CRC Press Taylor and Francis.
543 Mamy L., Patureau D., Barriuso E., Bedos C**.**, Bessac F., Louchart X., Martin-Laurent
544 F., Miege C., Benoit P., 2015. Prediction of the Fate of Organic Compounds in the
545 Environment From Their Molecular Properties: A Review. Critical Reviews in
546 Environmental Science and Technology 45, 1277-1377.
547 Martin-Laurent F., Sahnoun M.M., Merlin C., Vollmer G., Lübke M., 2014. Detection
548 and quantification of chlordecone in contaminated soils from the French West Indies
549 by GC-MS using the $^{13}C_{10}$-chlordecone stable isotope as tracer. Environ Sci Pollut
550 Res, 21, 4928–4933
551 Orndorff S.A., Colwell RR., 1980. Microbial transformation of kepone. Appl Environ
552 Microbiol, 39, 398–406.
553 PPDB (Pesticide properties database), 2013.
554 <http://sitem.herts.ac.uk/aeru/footprint/index2.htm>.
555 Regulation EC 1107/2009, 2009. Regulation (EC) No 1107/2009 of the European
556 Parliament and of the Council of 21 October 2009 concerning the placing of plant
557 protection products on the market and repealing Council Directives 79/ 117/EEC and
558 91/414/EEC.

559 Roberts T.R., Huston D.H., 1999. Metabolic Pathways of Agrochemicals Part 2
560 Insecticides and Fungicides. The Royal Society of Chemistry Information Services
561 Cambridge, UK.
562 Servien R., Mamy L., Li Z., Rossard V., Latrille E., Bessac F., Patureau D., Benoit P.,
563 2014. TyPol – A new methodology for organic compounds clustering based on their
564 molecular characteristics and environmental behaviour. Chemosphere, 111, 613-622.
565 Sakakibara F., Takagi K., Kataoka R., Kiyota H., Sato Y., Okada S., 2011. Isolation and
566 identification of dieldrin-degrading *Pseudonocardia* sp strain KSF27 using a soil-
567 charcoal perfusion method with aldrin trans-diol as a structural analog of dieldrin.
568 Biochem Biophys Res Commun, 411(1), 76–81.
569 Schanke C.A., Wackett L.P., 1992. Environmental reductive elimination reactions of
570 polychlorinated ethanes mimicked by transition-metal coenzymes. Environ. Sci.
571 Technol. 26: 830-833.
572 Subba-Rao R.V., Alexander M., 1985. Products formed from analogs of 1,1,1-trichloro-
573 2,2-bis-(p-chlorophenyl)ethane (DDT) TPs by Pseudomonas putida. Appl Environ
574 Microbiol 33:101–108.
575 Tenenhaus M., 1998. In: La regression, P.L.S. (Ed.), Théorie et Pratique. Technip,
576 Paris.
577 Wold S., 1978. Cross-validation estimation of the number of components in factor and
578 principal component analysis. Technometrics 24, 397– 405.
579

Table

Click here to download Table: Table Benoit_SI Pesticide Risk.docx

Table 1

Degradation reactions for different organochlorine pesticides and corresponding transformation products (TP). OX: Oxidation; EpOX: epoxidation; Hyox: hydroxylation; Rdn: reduction; Hygn: hydrogenation; Hys: hydrolysis; DeX: dehalogenation; R-DeCl: reactive dechlorination; Dehys: dehydrolysis; Phos: photolysis; ReAm: rearrangement. When there was no referenced CAS, a number was created according to the following format: CAS number of the parent-INRA-i (i represents the number of the degradation product among all degradation products of the parent compound)

Parent compound (PC)	CAS PC	Transformation product (TP)	CAS TP	OX	EpOX	HyOX	Rdn	Hygn	Hys	DeX	R-DeCl	Dehys	Phos	ReAm
DDT	50-29-3	DDD	72-54-8					x		x				
		p,,p'-DDE	72-55-9				x			x	x			
		4,4'-dichlorobenzophenone	90-98-2	x						x			x	
		4,4'-dichlorodiphenylacetic acid	90-98-2-INRA-1	x								x		
		bis(4-chlorophenyl)acetonitrile	50-29-3-INRA-1				x			x				
		DDMU	1022-22-6				x			x	x			
		4-chlorophenylacetic acid	1878-66-6	x		x								
		o,p'-DDE	3424-82-6				x			x	x			x
		1-(2-chlorophenyl)-1-(4-chlorophenyl)-2-choroethylene	50-29-3-INRA-2				x	x		x	x			x
		Dicofol	115-32-2	x		x								
Hexachlorobenzene	118-74-1	Pentachlorobenzene	608-93-5				x			x			x	
		1,2,3,4-tetrachlorobenzene	634-66-2				x			x				
		1,2,4,5-tetrachlorobenzene	95-94-3				x			x				
		1,2,3,5-tetrachlorobenzene	634-90-2				x			x			x	
		1,2,4-trichlorobenzene	120-82-1				x			x				
Endosulfan	115-29-7	Endosulfan diol	218-467-6						x					
		Endosulfan sulfate	1031-07-8						x					
		Endosulfan ether	33-69-52-6	x										
		Endosulfan hydroxyether	1021-19-8	x										
		Endosulfan lactone	3868-61-9	x										

Parent compound (PC)	CAS PC	Transformation product (TP)	CAS TP	OX	EpOX	HyOX	Rdn	Hygn	Hys	DeX	R-DeCl	Dehys	Phos	ReAm
Chlordane	57-74-9	Heptachlor	76-44-8							x	x			
		Heptachlor epoxide	1024-57-3	x	x									
		1-chloro-2-hydroxychlordene chlorohydrin	57-74-9-INRA-1			x			x	x				
		1-chloro-dihydrochlordene	57-74-9-INRA-2					x		x				
		3,4,5,6,7,8,8-heptachloro-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoindene-1,2-diol	57-74-9-INRA-3			x								
		1,2-dichlorochlordane	57-74-9-INRA-4									x		
		1-exo-hydroxy-2-chlorochlordene	57-74-9-INRA-5			x								
		Chlordene chlorohydrin	37571-87-2					x						
		Oxychlordane	27304-13-8	x	x									
Biphenyl	92-51-3	2-hydroxybiphenyl	90-43-7	x	x	x								
		3-hydroxybiphenyl	580-51-8	x	x	x								
		2,3-dihydro-2,3-dihydroxybiphenyl	34244-66-1	x					x					
		2,3-dihydroxybiphenyl	1133-63-7				x							
Heptachlor	76-44-8	1-hydroxychlordene	24009-05-0						x					
		Chlordene	3734-48-3							x				
		Chlordene epoxide	6058-23-7	x	x									
		Heptachlor epoxide	1024-57-3	x	x									
		3,4,5,6,7,8,8-heptachloro-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoindene-1,2-diol	57-74-9-INRA-3						x					
		1-hydroxy-2,3-epoxychlordene	1024-57-3-INRA-1						x					
g-HCH	608-73-1	Pentachlorcyclohexene	643-15-2				x			x	x			
		1,2,4-trichlorobenzene	120-82-1				x			x	x			
		1,4-dichlorobenzene	106-46-7							x				
		1,2,3-trichlorobenzene	87-61-6				x			x	x			
		1,2-dichlorobenzene	95-50-1							x				
		2,4,6-trichlorophenol	88-06-2							x	x			
		1,2,3,4-tetrachlorobenzene	634-66-2							x	x			

Parent compound (PC)	CAS PC	Transformation product (TP)	CAS TP	OX	EpOX	HyOX	Rdn	Hygn	Hys	DeX	R-DeCl	Dehys	Phos	ReAm
Chlordecone	143-50-0	10-hydrochlordecone	143-50-0-INRA-1				x				x			
		9-hydrochlordecone	143-50-0-INRA-2				x				x			
		6-hydrochlordecone	143-50-0-INRA-3				x				x			
		8-hydrochlordecone	143-50-0-INRA-4				x				x			
		cis-8,10-dihydrochlordecone	143-50-0-INRA-5				x				x			
		3,7-dihydrochlordecone	143-50-0-INRA-6				x				x			
		8,10,10-trihydrochlordecone	143-50-0-INRA-7				x				x			
		3,7,10-trihydrochlordecone	143-50-0-INRA-8				x				x			
		3,7,10,10-tetrahydrochlordecone	143-50-0-INRA-9				x				x			
		r-3,7,8,10-tetrahydrochlordecone	143-50-0-INRA-10				x				x			
		3,7,8,10,10-pentahydrochlordecone	143-50-0-INRA-11				x				x			
		2,3,7,8,10,10-hexahydrochlordecone	143-50-0-INRA-12				x				x			
		2,3,7,8,9,10,10-heptahydrochlordecone	143-50-0-INRA-13				x				x			
		1,2,3,7,8,9,10,10-Octahydrochlordecone	143-50-0-INRA-14				x				x			
		1,2,3,4,6,7,8,9,10-nonahydrochlordecone	143-50-0-INRA-15				x				x			
		2,3,4,6,7,8,9,10,10-nonahydrochlordecone	143-50-0-INRA-16				x				x			
		1,2,3,6,7,8,9,10,10-nonahydrochlordecone	143-50-0-INRA-17				x				x			
		1,3,4,6,7,8,9,10,10-nonahydrochlordecone	143-50-0-INRA-18				x				x			
		Decahydrochlordecone	143-50-0-INRA-19				x				x			
		Chlordecol	143-50-0-INRA-20	x		x					x			

Table 2

Chlorinated compounds inputted in TyPol with CAS numbers, names, chemical formulae and chemical families. The parent CAS is given in case of transformation products (PCB: polychlorinated biphenyls, PCDF: polychlorinated dibenzofurans, PCDD: polychlorinated dibenzodioxins).

CAS	Name	Chemical formula	Chemical family	Parent CAS
115-29-7	Endosulfan	$C_9H_6C_{l6}O_3S$	Organochlorine	
1031-07-8	Endosulfan sulfate	$C_9H_6C_{l6}O_4S$	Organochlorine	115-29-7
118-74-1	Hexachlorobenzene	C_6Cl_6	Organochlorine	
143-50-0	Chlordecone	C10Cl10O	Organochlorine	
143-50-0-INRA-1	10-Hydrochlordecone	C10HCl9O	Organochlorine	143-50-0
143-50-0-INRA-10	r-3,7,8,t,10-Tetrahydrochlordecone	C10H4Cl6O	Organochlorine	143-50-0
143-50-0-INRA-11	3,7,8,10,10-Pentahydrochlordecone	C10H5Cl5O	Organochlorine	143-50-0
143-50-0-INRA-12	2,3,7,8,10,10-Hexahydrochlordecone	C10H6Cl4O	Organochlorine	143-50-0
143-50-0-INRA-13	2,3,7,8,9,10,10-Heptahydrochlordecone	C10H7Cl3O	Organochlorine	143-50-0
143-50-0-INRA-14	1,2,3,7,8,9,10,10-Octahydrochlordecone	C10H8Cl2O	Organochlorine	143-50-0
143-50-0-INRA-15	1,2,3,4,6,7,8,9,10-Nonahydrochlordecone	C10H9Cl1O	Organochlorine	143-50-0
143-50-0-INRA-16	2,3,4,6,7,8,9,10,10-Nonahydrochlordecone	C10H9Cl1O	Organochlorine	143-50-0
143-50-0-INRA-17	1,2,3,6,7,8,9,10,10-Nonahydrochlordecone	C10H9Cl1O	Organochlorine	143-50-0
143-50-0-INRA-18	1,3,4,6,7,8,9,10,10-Nonahydrochlordecone	C10H9Cl1O	Organochlorine	143-50-0
143-50-0-INRA-19	Decahydrochlordecone	C10H10O	Organochlorine	143-50-0
143-50-0-INRA-2	9-Hydrochlordecone	C10HCl9O	Organochlorine	143-50-0
143-50-0-INRA-20	Chlordecol	C10H2Cl10O	Organochlorine	143-50-0
143-50-0-INRA-3	6-Hydrochlordecone	C10HCl9O	Organochlorine	143-50-0
143-50-0-INRA-4	8-Hydrochlordecone	C10HCl9O	Organochlorine	143-50-0
143-50-0-INRA-5	cis-8,10-Dihydrochlordecone	C10H2Cl8O	Organochlorine	143-50-0
143-50-0-INRA-6	3,7-Dihydrochlordecone	C10H2Cl8O	Organochlorine	143-50-0
143-50-0-INRA-7	8,10,10-Trihydrochlordecone	C10H3Cl7O	Organochlorine	143-50-0
143-50-0-INRA-8	3,7,10-Trihydrochlordecone	C10H3Cl7O	Organochlorine	143-50-0
143-50-0-INRA-9	3,7,10,10-Tetrahydrochlordecone	C10H4Cl6O	Organochlorine	143-50-0
2385-85-5	Mirex	C10Cl12	Organochlorine	
4234-79-1	Kelevan	C17H12Cl10O4	Organochlorine	
50-29-3	p,p'-DDT	C14H9Cl5	Organochlorine	
72-54-8	DDD	C14H10Cl4	Organochlorine	50-29-3
72-55-9	DDE	C14H8Cl4	Organochlorine	50-29-3
58-89-9	Lindane	C6H6Cl6	Organochlorine	
608-73-1	Hexachlorocyclohexane	C6H6Cl6	Organochlorine	
107534-96-3	Tebuconazole	C16H22ClN3O	Triazole	
107534-96-3-INRA-1	M1-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-10	M10-Tebuconazole	C16H22ClN3O3	Triazole metabolite	107534-96-3
107534-96-3-INRA-11	M11-Tebuconazole	C16H20ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-12	M12-Tebuconazole	C16H20ClN3O2	Triazole metabolite	107534-96-3

107534-96-3-INRA-13	M13-Tebuconazole	C16H20ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-14	M14-Tebuconazole	C16H20ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-16	M16-Tebuconazole	C16H20ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-2	M2-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-24	M24-Tebuconazole	C15H20ClN3O	Triazole metabolite	107534-96-3
107534-96-3-INRA-25	M25-Tebuconazole	C13H16ClN3O	Triazole metabolite	107534-96-3
107534-96-3-INRA-26	M26-Tebuconazole	C12H14ClN3O	Triazole metabolite	107534-96-3
107534-96-3-INRA-3	M3-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-4	M4-Tebuconazole	C16H22ClN3O3	Triazole metabolite	107534-96-3
107534-96-3-INRA-5	M5-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-6	M6-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-65	M65-Tebuconazole	C15H21ClN2O	Triazole metabolite	107534-96-3
107534-96-3-INRA-67	M67-Tebuconazole	C15H21ClN2O	Triazole metabolite	107534-96-3
107534-96-3-INRA-7	M7-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-76	M76-Tebuconazole	C7H5ClO2	Triazole metabolite	107534-96-3
107534-96-3-INRA-8	M8-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
107534-96-3-INRA-9	M9-Tebuconazole	C16H22ClN3O2	Triazole metabolite	107534-96-3
119446-68-3	Difenoconazole	C19H17Cl2N3O3	Triazole	
131983-72-7	Triticonazole	C17H20ClN3O	Triazole	
131983-72-7-INRA-1	(1R,3R,E)-3-(4-chlorobenzylidene)-5,5-dimethyl-1-((1H)-1,2,4-triazol-1-ylmethyl)-cyclopentan-1,3-diol	C17H20ClN3O2	Triazole metabolite	131983-72-7
131983-72-7-INRA-2	(E)-2-(4-chlorobenzylidene)-5,5-dimethyl-1-((1H)-1,2,4-triazol-1-ylmethyl)-cyclopentan-1,3-diol	C17H20ClN3O2	Triazole metabolite	131983-72-7
133855-98-8	Epoxiconazole	C17H13ClFN3O	Triazole	
94361-06-5	Cyproconazole	C15H18ClN3O	Triazole	
14168-01-5	Dilor	C10H7Cl7	Chloro-bicycloheptene	
1715-40-8	Bromocyclene	C8H5BrCl6	Chloro-bicycloheptene	
2550-75-6	Chlorbicyclene	C9H6Cl8	Chloro-bicycloheptene	
297-78-9	Isobenzane	C9H4Cl8O	Chloro-bicycloheptene	
309-00-2	Aldrine	C12H8Cl6	Chloro-bicycloheptene	
465-73-6	Isodrine	C12H8Cl6	Chloro-bicycloheptene	
57-74-9	Chlordane	C10H6Cl8	Chloro-bicycloheptene	
27304-13-8	Oxychlordane	C10H4Cl8O	Chloro-bicycloheptene metabolite	57-74-9
60-57-1	Dieldrine	C12H8Cl6O	Chloro-bicycloheptene	
76-44-8	Heptachlore	C10H5Cl7	Chloro-bicycloheptene	
1024-57-3	Heptachlore epoxide	C10H5Cl7O	Chloro-bicycloheptene	76-44-8, 57-74-9
8001-35-2	Toxaphene	C10H8Cl8	Chloro-bicycloheptene	
15972-60-8	Alachlor	C14H20ClNO2	Chloroacetamide	
1918-16-7	Propachlor	C11H14ClNO	Chloroacetamide	
34256-82-1	Acetochlor	C14H20ClNO2	Chloroacetamide	
51218-45-2	Metolachlor	C15H22ClNO2	Chloroacetamide	
67129-08-2	Metazachlor	C14H16ClN3O	Chloroacetamide	
122-34-9	Simazine	C7H12ClN5	Triazine	

1912-24-9	Atrazine	C8H14ClN5	Triazine	
21725-46-2	Cyanazine	C9H13ClN6	Triazine	
5915-41-3	Terbuthylazine	C9H16ClN5	Triazine	
15545-48-9	Chlortoluron	C10H13ClN2O	Urea	
1746-81-2	Monolinuron	C9H11ClN2O2	Urea	
330-55-2	Linuron	C9H10Cl2N2O2	Urea	
555-37-3	Neburon	C12H16Cl2N2O	Urea	
330-54-1	Diuron	C9H10Cl2N2O	Phenylurea	
95-76-1	3,4-dichloroaniline	C6H5Cl2N	Phenylurea metabolite	330-54-1
2327-02-8	3,4-dichlorophenyl urea	C7H6Cl2N2O	Phenylurea metabolite	330-54-1
3567-62-2	1-(3,4-dichlorophenyl)-3-methylurea	C8H8Cl2N2O	Phenylurea metabolite	330-54-1
52315-07-8	Cypermethrin	C22H19Cl2NO3	Pyrethroid	
52645-53-1	Permethrin	C21H20Cl2O3	Pyrethroid	
68359-37-5	Cyfluthrin	C22H18Cl2FNO3	Pyrethroid	
68359-37-5-INRA-1	3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid	C8H10Cl2O2	Pyrethroid metabolite	68359-37-5
32809-16-8	Procymidone	C13H11Cl2NO2	Dicarboximide	
36734-19-7	Iprodione	C13H13Cl2N3O3	Dicarboximide	
63637-89-8	N-(3,5-dichlorophenyl)3-isopropyl-2,4-dioxoimidazoline-1-carboxamide	C17H20ClN3O2	Dicarboximide metabolite	36734-19-7
7085-19-0	Mecoprop	C10H11ClO3	Aryloxyalkanoic acid	
94-74-6	MCPA	C9H9ClO3	Aryloxyalkanoic acid	
1570-64-5	2-methyl-4-chlorophenol	C7H7ClO	Aryloxyalkanoic acid metabolite	94-74-6
1698-60-8	Chloridazon	C10H8ClN3O	Pyridazinone	
27314-13-2	Norflurazon	C12H9ClF3N3O	Pyridazinone	
23576-24-1	Desmethyl norflurazon	C11H7ClF3N3O	Pyridazinone metabolite	27314-13-2
133-06-2	Captan	C9H8Cl3NO2S	Phthalimide	
133-07-3	Folpet	C9H4Cl3NO2S	Phthalimide	
175013-18-0	Pyraclostrobin	C19H18ClN3O4	Strobilurin	
361377-29-9	Fluoxastrobin	C21H16ClFN4O5	Strobilurin	
2303-16-4	Di-allate	C10H17Cl2NOS	Thiocarbamate	
2303-17-5	Tri-allate	C10H16Cl3NOS	Thiocarbamate	
1897-45-6	Chlorothalonil	C8Cl4N2	Chloronitrile	
1897-45-6-INRA-1	4-hydroxy-2,5,6-trichloroisophtalonitrile	C8HCl3N2O	Chloronitrile metabolite	1897-45-6
335104-84-2	Tembotrione	C17H16ClF3O6S	Triketone	
99105-77-8	Sulcotrione	C14H13ClO5S	Triketone	
94-75-7	2,4-D	C8H6Cl2O3	Alkylchlorophenoxy	
709-98-8	Propanil	C9H9Cl2NO	Anilide	
51338-27-3	Diclofop-methyl	C16H14Cl2O4	Aryloxyphenoxypropionate	
23950-58-5	Propyzamide	C12H11Cl2NO	Benzamide	
1918-00-9	Dicamba	C8H6Cl2O3	Benzoic acid	
101-21-3	Chlorpropham	C10H12ClNO2	Carbamate	
74070-46-5	Aclonifen	C12H9ClN2O3	Diphenyl ether	
16672-87-0	Ethephon	C2H6ClO3P	Ethylene generator	
126833-17-8	Fenhexamid	C14H17Cl2NO2	Hydroxyanilide	

110488-70-5	Dimethomorph	C21H22ClNO4	Morpholine
135410-20-7	Acetamiprid	C10H11ClN4	Neonicotinoid
5598-13-0	Chlorpyrifos-methyl	C7H7Cl3NO3PS	Organophosphate
1918-02-1	Picloram	C6H3Cl3N2O2	Pyridine
64902-72-3	Chlorsulfuron	C12H12ClN5O4S	Sulfonylurea
13029-08-8	2,2’-Dichlorobiphenyle	C12H8Cl2	PCB
16605-91-7	2,3-Dichlorobiphenyle	C12H8Cl2	PCB
2050-67-1	3,3’-Dichlorobiphenyle	C12H8Cl2	PCB
2050-68-2	4,4’-Dichlorobiphenyle	C12H8Cl2	PCB
2051-24-3	Decachlorobiphenyle	C12Cl10	PCB
2051-60-7	2-Chlorobiphenyle	C12H9Cl	PCB
2051-61-8	3-Chlorobiphenyle	C12H9Cl	PCB
25569-80-6	2,3’-Dichlorobiphenyle	C12H8Cl2	PCB
2974-90-5	3,4’-Dichlorobiphenyle	C12H8Cl2	PCB
2974-92-7	3,4-Dichlorobiphenyle	C12H8Cl2	PCB
33146-45-1	2,6-Dichlorobiphenyle	C12H8Cl2	PCB
33284-50-3	2,4-Dichlorobiphenyle	C12H8Cl2	PCB
34883-39-1	2,5-Dichlorobiphenyle	C12H8Cl2	PCB
34883-41-5	3,5-Dichlorobiphenyle	C12H8Cl2	PCB
34883-43-7	2,4’-Dichlorobiphenyle	C12H8Cl2	PCB
35065-30-6	2,2’,3,3’,4,4’,5-Heptachlorobiphenyle	C12H3Cl7	PCB
35694-08-7	2,2’,3,3’,4,4’,5,5’-Octachlorobiphenyle	C12H2Cl8	PCB
37680-66-3	2,2’,4-Trichlorobiphenyle	C12H7Cl3	PCB
38380-07-3	2,2’,3,3’,4,4’-Hexachlorobiphenyle	C12H4Cl6	PCB
38444-78-9	2,2’,3-Trichlorobiphenyle	C12H7Cl3	PCB
38444-93-8	2,2’,3,3’-Tetrachlorobiphenyle	C12H6Cl4	PCB
40186-72-9	2,2’,3,3’,4,4’,5,5’,6-Nonachlorobiphenyle	C12HCl9	PCB
52663-59-9	2,2’,3,4-Tetrachlorobiphenyle	C12H6Cl4	PCB
52663-62-4	2,2’,3,3’,4-Pentachlorobiphenyle	C12H5Cl5	PCB
52663-71-5	2,2’,3,3’,4,4’,6-Heptachlorobiphenyle	C12H3Cl7	PCB
52663-78-2	2,2’,3,3’,4,4’,5,6-Octachlorobiphenyle	C12H2Cl8	PCB
52663-79-3	2,2’,3,3’,4,4’,5,6,6’-Nonachlorobiphenyle	C12HCl9	PCB
55215-18-4	2,2’,3,3’,4,5-Hexachlorobiphenyle	C12H4Cl6	PCB
60145-20-2	2,2’,3,3’,5-Pentachlorobiphenyle	C12H5Cl5	PCB
39001-02-0	OCDF	C12Cl8O	PCDF
51207-31-9	2,3,7,8-TCDF	C12H4Cl4O	PCDF
55673-89-7	1,2,3,4,7,8,9-HpCDF	C12HCl7O	PCDF
57117-31-4	2,3,4,7,8-PeCDF	C12H3Cl5O	PCDF
57117-41-6	1,2,3,7,8-PeCDF	C12H3Cl5O	PCDF
57117-44-9	1,2,3,6,7,8-HxCDF	C12H2Cl6O	PCDF
60851-34-5	2,3,4,6,7,8-HxCDF	C12H2Cl6O	PCDF
67562-39-4	1,2,3,4,6,7,8-HpCDF	C12HCl7O	PCDF
70648-26-9	1,2,3,4,7,8-HxCDF	C12H2Cl6O	PCDF

72918-21-9	1,2,3,7,8,9-HxCDF	C12H2Cl6O	PCDF
1746-01-6	2,3,7,8-Tetrachlorodibenzo-p-dioxine	C12H4Cl4O2	PCDD
19408-74-3	1,2,3,7,8,9-HxCDD	C12H2Cl6O2	PCDD
3268-87-9	OCDD	C12Cl8O2	PCDD
35822-46-9	1,2,3,4,6,7,8-HpCDD	C12HCl7O2	PCDD
39227-28-6	1,2,3,4,7,8-HxCDD	C12H2Cl6O2	PCDD
40321-76-4	1,2,3,7,8-PeCDD	C12H3Cl5O2	PCDD
57653-85-7	1,2,3,6,7,8-HxCDD	C12H2Cl6O2	PCDD

Figure captions

Fig. 1.

Graphical representation of the obtained clusters in the two X-axes of the PLS with the molecular descriptors and environmental parameters on all organochlorine compounds – with exception of the putative transformation products of chlordecone for which environmental parameters are unknown.

Fig. 2.

Circles of correlations of the 'environmental parameters' (in blue) and 'molecular descriptors' (in red) variables on the two main components of the PLS (Comp 1 and Comp 2). C.i–i stands for the connectivity index C.i of order i (i = 0 to 5), and V.c-i stands for the valence connectivity index V.c of order i (i = 0–5).

Fig. 3.

Range of variation (box-and-whisker plots) of the values of the seven 'environmental parameters' considered into TyPol (water solubility *Sw*, octanol–water partition coefficient *Kow*, vapor pressure P_{vap}, Henry's law constant K_H, adsorption coefficient normalized to soil carbon organic content *Koc*, half-life *DT50*, and bioconcentration factor *BCF*) for each cluster after analysis of the 130 chlorinated compounds. Dotted lines represent the limits between: volatile (logP_{vap} > 1) and non-volatile compounds (logP_{vap} < 1) (FOCUS, 2008); mobile (log*Koc* < 2.7) and non-mobile compounds (log*Koc* > 2.7) (McCall et al., 1980); persistent (log*DT50* > 2.25) and non-persistent compounds (log*DT50* < 2.25) (Regulation EC 1107/2009, 2009), and compounds having (log*BCF* > 2) or not (log*BCF* < 2) a potential of bioaccumulation (Regulation EC 1107/ 2009, 2009).

Fig. 4.

Circles of correlations of the 'molecular descriptors' (in red) variables on the two main components of the PLS (Comp 1 and Comp 2). C.i–i stands for the connectivity index C.i of order i (i = 0 to 5), and V.c-i stands for the valence connectivity index V.c of order i (i = 0–5). PLS realized with the molecular descriptors only – considering all organochlorine compounds including the putative metabolites of chlordecone.

Fig. 5.

Graphical representation of the clusters obtained with the ‘molecular descriptors’ only – considering all organochlorine compounds including the putative metabolites of chlordecone.

Fig. 6.

Filiation’s parents-TPs shown on the cluster representation obtained with the molecular descriptors only

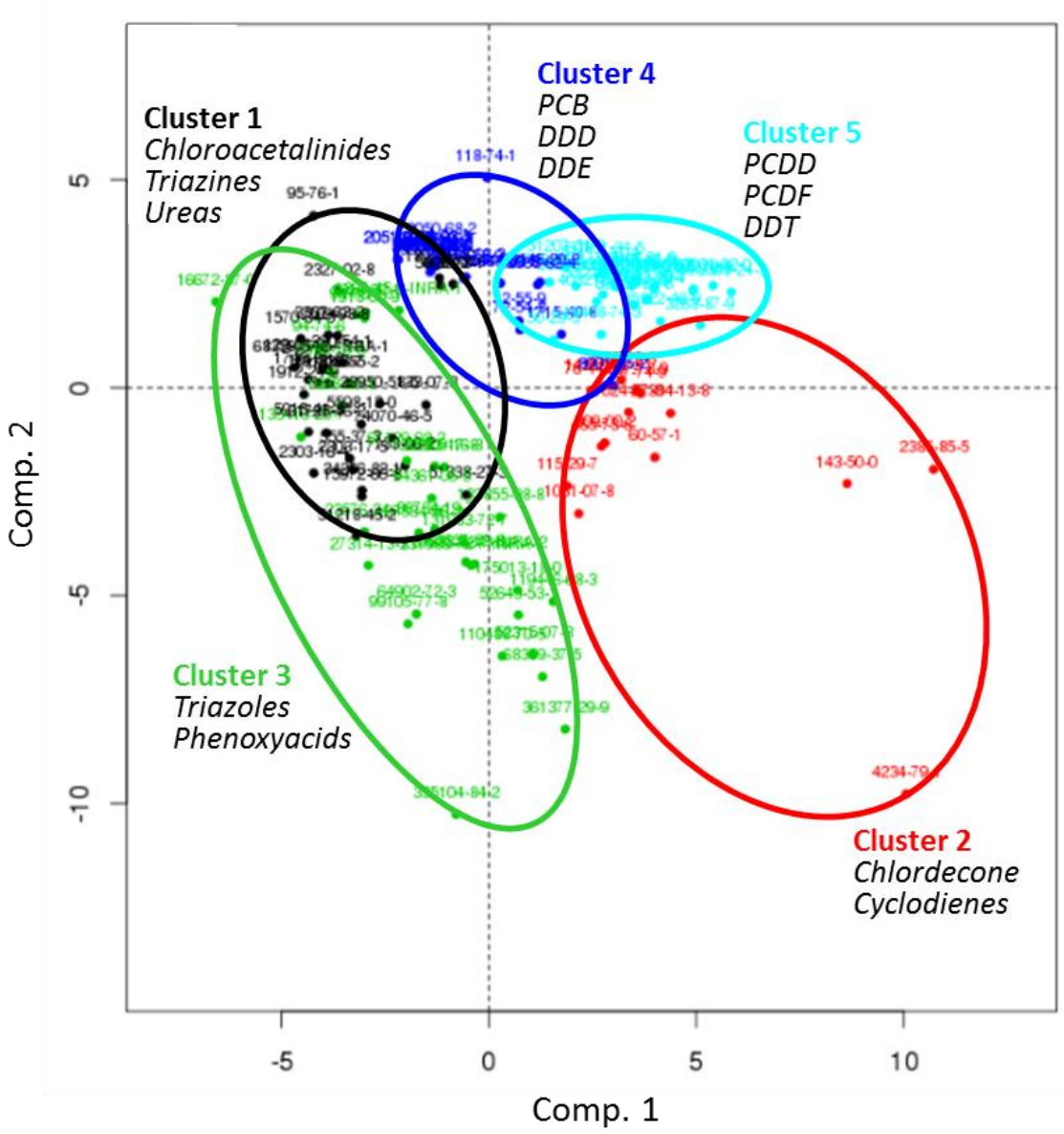

Cluster 1
Chloroacetalinides
Triazines
Ureas
Cluster 4
PCB
DDD
DDE
Cluster 5
PCDD
PCDF
DDT
Cluster 3
Triazoles
Phenoxyacids
Cluster 2
Chlordecone
Cyclodienes
Comp. 1
Comp. 2
-5
0
5
10
-10
-5
0
5

Fig. 1

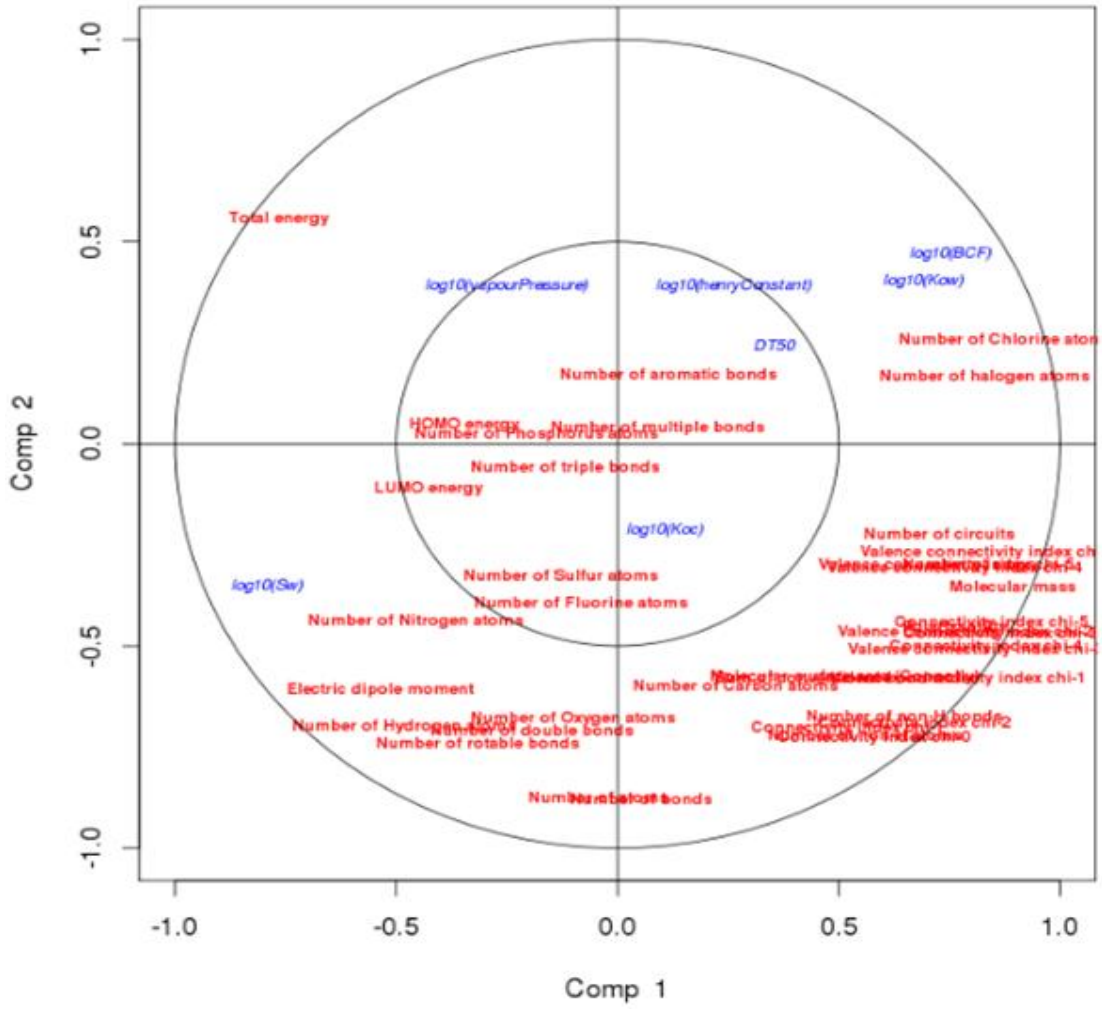

Comp 2
Comp 1
1.0
0.5
0.0
-0.5
-1.0
Total energy
log10(BCF)
log10(Kow)
log10(vapourPressure)
log10(henryConstant)
DT50
Number of Chlorine aton
Number of halogen atoms
Number of aromatic bonds
HOMO energy
Number of multiple bonds
Number of triple bonds
LUMO energy
log10(Koc)
Number of circuits
Molecular mass
log10(Sw)
Number of Sulfur atoms
Number of Fluorine atoms
Number of Nitrogen atoms
Electric dipole moment
Number of Carbon atoms
Number of Oxygen atoms
Number of double bonds
Number of rotable bonds

Fig. 2

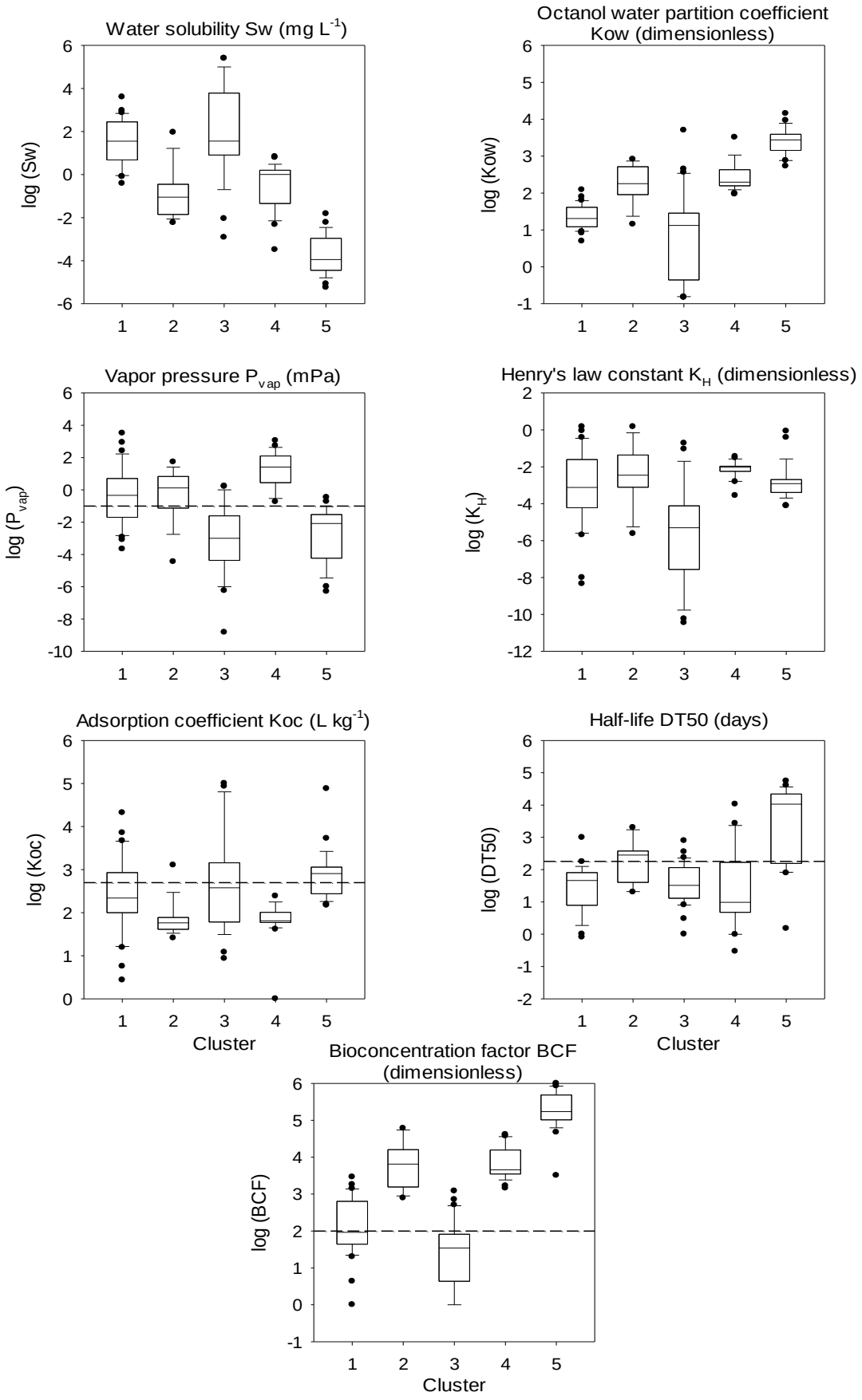

Water solubility Sw (mg L-1)
log (Sw)
Octanol water partition coefficient Kow (dimensionless)
log (Kow)
Vapor pressure Pvap (mPa)
log (Pvap)
Henry's law constant KH (dimensionless)
log (KH)
Adsorption coefficient Koc (L kg-1)
log (Koc)
Half-life DT50 (days)
log (DT50)
Cluster
Bioconcentration factor BCF (dimensionless)
log (BCF)
Cluster

Fig. 3

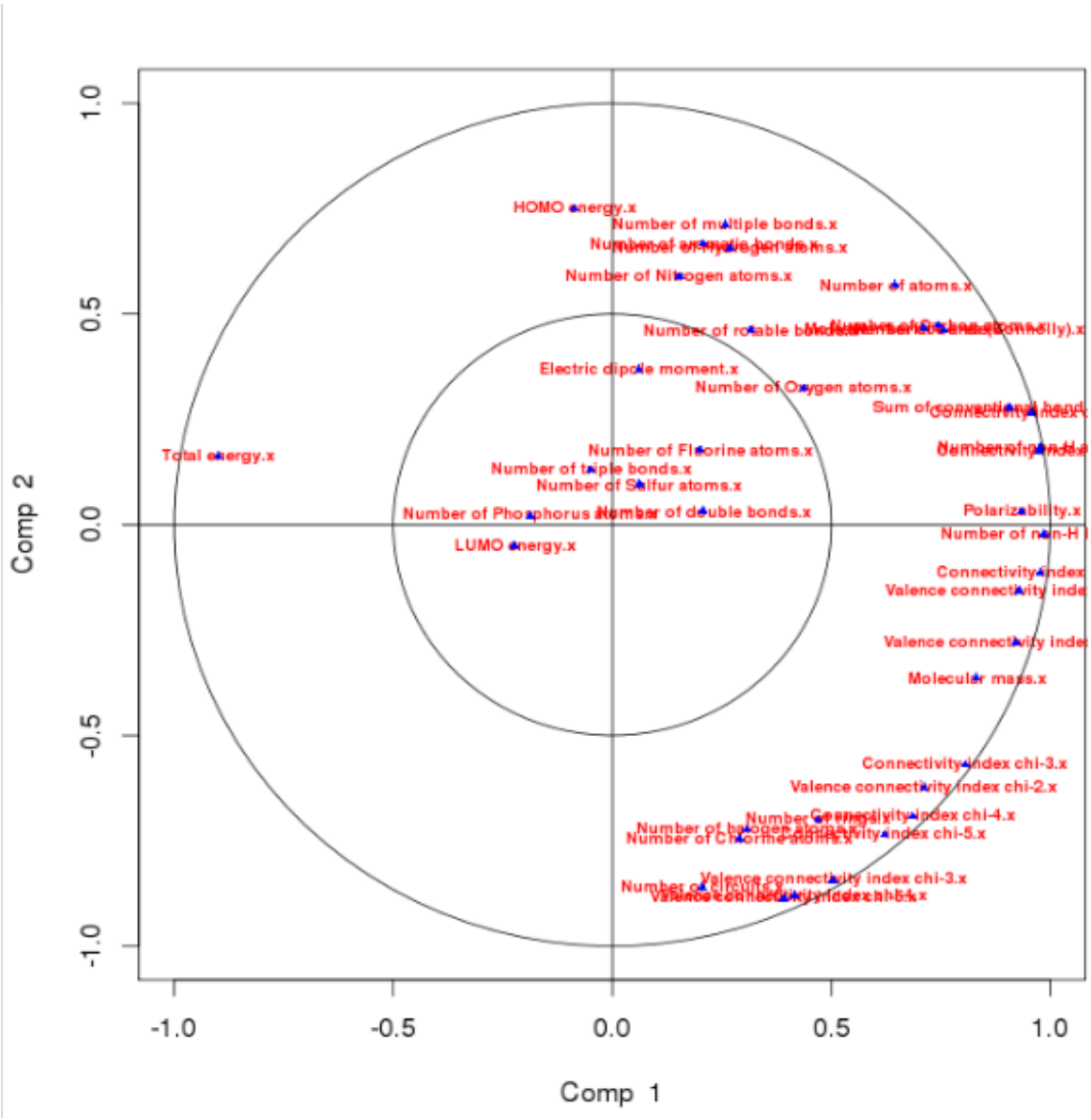

HOMO energy.x
Number of multiple bonds.x
Number of Nitrogen atoms.x
Number of atoms.x
Electric dipole moment.x
Number of Oxygen atoms.x
Total energy.x
Number of Fluorine atoms.x
Number of triple bonds.x
Number of Sulfur atoms.x
Number of double bonds.x
LUMO energy.x
Polarizability.x
Valence connectivity inde
Molecular mass.x
Connectivity index chi-3.x
Valence connectivity index chi-2.x
Valence connectivity index chi-5.x
Valence connectivity index chi-3.x
Comp 2
Comp 1
1.0
0.5
0.0
-0.5
-1.0
-1.0
-0.5
0.0
0.5
1.0

Fig. 4

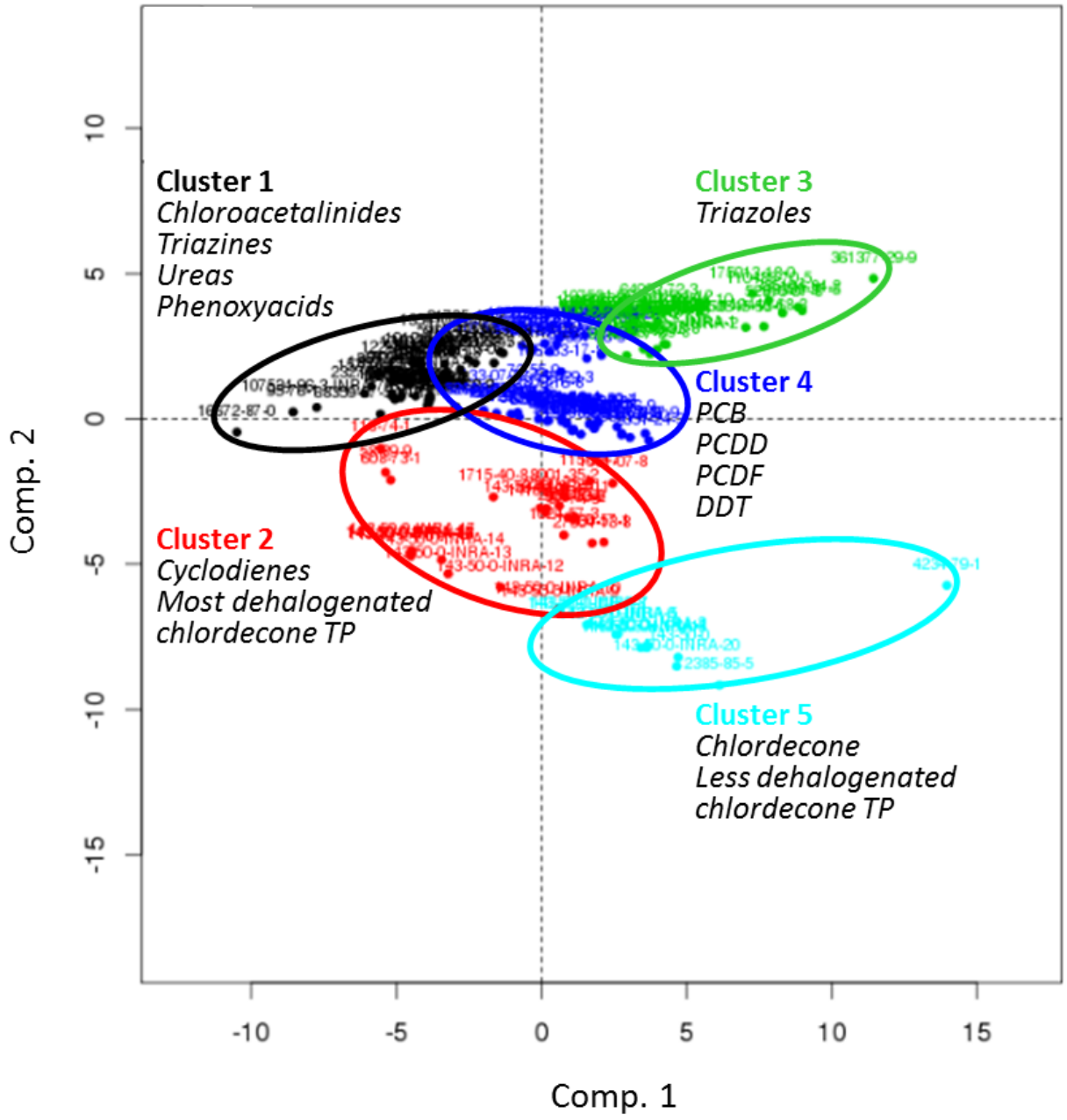

Cluster 1
Chloroacetalinides
Triazines
Ureas
Phenoxyacids
Cluster 3
Triazoles
Cluster 4
PCB
PCDD
PCDF
DDT
Cluster 2
Cyclodienes
Most dehalogenated
chlordecone TP
Cluster 5
Chlordecone
Less dehalogenated
chlordecone TP
Comp. 1
Comp. 2
10
5
0
-5
-10
-15
-10
-5
0
5
10
15

Fig. 5

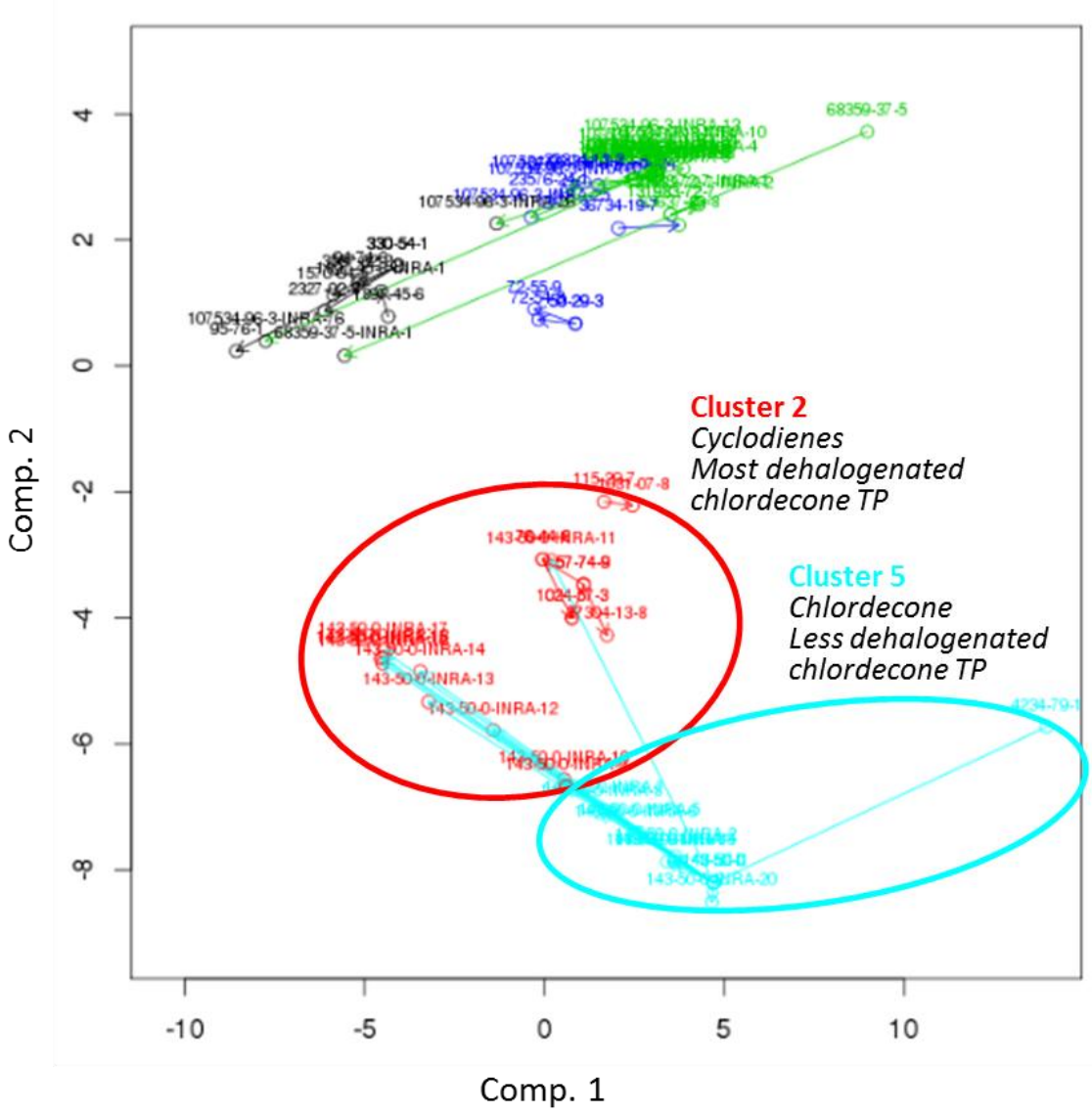

Cluster 2
Cyclodienes
Most dehalogenated
chlordecone TP
Cluster 5
Chlordecone
Less dehalogenated
chlordecone TP
Comp. 1
Comp. 2
-10
-5
0
5
10
4
2
0
-2
-4
-6
-8

Fig. 6